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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,424	11/24/2003	Sang-Wha Lee	NEIT0018	6330

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EXAMINER	
SALMON, KATHERINE D	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/720,424	LEE ET AL.	
	Examiner	Art Unit	
	Katherine Salmon	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *5-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed 8/23/2006. Currently Claims 1-19 are pending. Claims 5-18 have been withdrawn. Claims 1-4 and 19 and SEQ IDs 1 and 8 are currently under examination.

2. The following rejections are reiterated. Response to arguments follows.

3. This action is FINAL.

Petition

4. The Petition for rejoining the nucleotide sequences under 37 C.F.R. 1.144 was received on 7/31/2006. The petition under 37 C.F.R. 1.144 for rejoinder of ten primers has been denied (see Petition Decision filed 10/18/2006).

Reiterated Rejections

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5474796 December 12, 1995).

Claims 1-3 are drawn to a sequence which is "fully complementary" to SEQ ID 1 or a sequence which is "fully complementary" to SEQ ID 8. The instant specification provides no guidelines as to what is encompassed by a sequence, which is "fully

complementary" to SEQ ID No. 1 or "fully complementary" to SEQ ID NO. 8. Broadly interpreted this could mean a sequence which is only a fragment of SEQ ID No. 1 or 8 but which complements fully. Brennan teaches every possible permutation of a 10-mer oligonucleotide (see Column 9, lines 53-55). Therefore, since Brennan teaches every possible combination of a 10 mer, Brennan inherently teaches 10mer combinations which are "fully complement" SEQ ID NO 1 and SEQ ID No. 8.

Response to Arguments

The response traverses the rejection. The response asserts that based on Phillips v. AWH Corporation, 415 F. 3d 1303 (Fed. Cir. 2005) claims must be read in view of the specification as it would be interpreted by one of ordinary skill in the art (p. 3 1st full paragraph). The response asserts there is no indication in the instant specification that fragment of sequences complimentary to SEQ ID No. 1 and 8 are intended (p. 3 1st full paragraph). The response asserts a person of ordinary skill in the art would interpret the phrase "a sequence which is fully complementary" as being the same length as the original sequence and comprised of nucleotides that are complimentary to the nucleotides in the same position in the original sequence (p. 3 1st full paragraph). These arguments have been thoroughly reviewed but are not found persuasive.

Though, the claims are read in light of the specification, the specification gives no specific definition of fully complementary. The response asserts a specific interpretation

of "a sequence, which is fully complementary" as the only interpretation of "fully complementary" that one of skill in the art would use. Though the interpretation presented in the reply is one of the interpretations of "a sequence, which is fully complementary" it is not the only interpretation of the phrase. The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *in re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *in re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111). The claims are given the broadest reasonable interpretation consistent with the indefinite claim language and specification wherein the "a sequence which is fully complementary" can be interpreted broadly as any sequence which complements at least part of SEQ ID 1 or 8 and is 100% complementary at the overlapped region. Therefore a 10 mer of SEQ ID NO. 1 or 8 which was 100% complementary would be encompassed by the broad claim language. The phrase "a sequence which is fully complementary" does not limit the complement fragments to only sequences, which complement every nucleotide of SEQ ID No. 1 or 8. The phrase "the complement of SEQ ID No." would be interpreted as a sequence, which was the complement of a SEQ ID, which spanned the whole SEQ ID and was complementary at every nucleotide position.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 2, 3, 4, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gravitt et al (Journal of Clinical Microbiology January 2000 Vol 38 p. 357) in view of Chan et al (Journal of Virology May 1995 Vol 69 p. 3074) and Gelfand et al (US Patent 5487972 January 30,1996).

Gravitt et al. teaches the improvement of consensus PCR primers to detect a wide variety of HPV genotypes. Gravitt et al teaches primers designed in a conserved region of the L1 open reading frame can be used to detect various genotypes of HPV (p. 357 2nd column 1st paragraph). Gravitt et al teaches the L1 region of all sequence

HPV genotypes was used to design primers (p. 358 Materials and Methods HPV sequence alignment and primer design). Gravitt et al teaches in designing primers, the efficiency of amplification is related to the number, position, and stability of a mismatch (p. 358 Results 1st paragraph). Gravitt et al. teaches primers with greater than four mismatches were less efficient (p. 358 Results 1st paragraph). Gravitt et al. teaches primers with less than four mismatches overall but with one or more mismatches at the 3' end of the oligonucleotide were less efficient (p. 358 Results 1st paragraph). Gravitt et al teaches that the concentration of magnesium chloride in the PCR assay would affect the ability of primer pairs to detect genotypes (p. 358 Results last sentence and first sentence of p. 359). Gravitt et al teaches the use of primers designed to nondiscriminately amplify any genital HPV type present in a reaction mixture (p. 361 2nd paragraph). With regard to Claim 19, Gravitt et al. teaches the use of a PCR assay comprising primers, a mixture of dNTPs, taq polymerase, and a PCR buffer.

Gravitt et al., however, does not teach the alignment of other genes of HPV genotypes or guidance in choosing primers which have been designed.

Chan et al teaches the phylogenic relationship of all known papillomaviruses and a database which encompasses HPV-1 to HPV-73 (Abstract). Chan et al. teaches that a new HPV genotype is one that has at least 10% dissimilarity in the combined nucleotide sequences of the E6, E7, and L1 genes when compared with known genotypes (p. 3074 2nd column 1st paragraph). Chan et al teaches the sequencing of 2.4 kb or the genome of all new isolates and sequence alignment (p. 3074 2nd column 1st paragraph). Chan et al teaches the alignment of several genomic segments among

all known PV genomes (p. 3075 2nd column Results 1st paragraph). Chan et al teaches the alignment of the amino acid sequences, which correspond to the L1 gene of 92 PV types (p. 3075 2nd column Results 2nd paragraph and Figure 1).

Gelfand et al. teaches a process of detecting a target nucleic acid using primers and probes in a PCR amplification assay (abstract). Gelfand et al. teaches a method comprising providing a set of oligonucleotide primers and amplifying the target nucleic acid sequence in a PCR reaction annealing both the primers and a labeled probe, and detecting the release of labeled fragments to determine the presence or absence of target sequences in the sample (column 2, lines 46-67 and column 3 lines 1-10).

Gelfand et al. provides guidance in the choosing of primers.

"The primer must be sufficiently long to prime the synthesis of extension products in the presences of the agent for polymerization. The exact length and composition of the primer will depend on many factors, including temperature of the annealing reaction, source and composition of the primer, proximity of the probe annealing site to the primer annealing site, and ration of primer: probe concentration. For example, depending on the complexity of the target sequence, the oligonucleotide primer typically contains about 15-30 nucleotides, although a primer may contain more or fewer nucleotides. The primers must be sufficiently complementary to anneal to their respective strands selectively and form stable duplexes" (Column 8 lines 21-34).

With regard to Claim 19, Gelfand et al. teaches a kit which includes primers, suitable packaged reagents and materials needed for amplification, buffers, and dNTPs (Column 14, lines 5-10).

Therefore, the ordinary artisan would have been motivated to select any number of primers including SEQ ID Nos. 1 and 8 for amplifying a region of HPV which could be use to identify a large number of genotypes of HPV. The art of designing primers at the time the invention was made was very well described in the art. The art uses alignment

programs to align sequences of interest and then uses algorithms to select and test primers for their desired function of either detecting or distinguishing particular organisms. Designing primers, which are equivalents to those taught in the art, is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as primers, see Gelfand et al. Moreover there are many Internet web sites that provide free downloadable software to aid in the selection of primers drawn from genetic data recorded in a spreadsheet. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design primers. The claimed primers are prima facie obvious over the cited references in the absence of secondary considerations, given the extensive teachings in the art. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the multiple alignment and oligonucleotides taught by Gravitt et al. and Chan et al. to create new primers and using the guidance of the design constraints of primers taught by Gelfand et al. to obtain equivalent alternative primers of the claimed invention. The ordinary artisan would be motivated to have designed and test new primers to obtain additional oligonucleotides that function to detect HPV genotypes and identify oligonucleotides with improved properties.

Response to Arguments

The response traverses the rejection. The response asserts that the preceding rejection is an "obvious to try" not an obviousness rejection (p. 4 1st paragraph). The reply points to In re Fine and In re Geiger (p. 4 1st paragraph). The reply asserts the art does not teach or suggest the specific sequences identified as SEQ ID No. 1 and 8 and sequences fully complimentary (p. 4 1st paragraph). The reply asserts that none of the cited references mentions primer sequences, which do not contain degenerate nucleotides (p. 4 1st full paragraph). The reply asserts even aligning the L1 regions among the HPV types in order to design primers that can amplify various HPV genotypes can result in primer sequences with a lot of degenerate nucleotides and that it is not routine for the ordinary artisan to select primer sequences that do not contain any degenerate nucleotides from all the possible primer sequences (p. 4 1st full paragraph). These arguments have been thoroughly reviewed but are not found persuasive.

Applicant argues that there is no reasonable expectation of success, that the art is rather an "obvious to try". The MPEP 2144.08 states "obviousness does not require absolute predictability, only a reasonable expectation of success; i.e., a reasonable expectation of obtaining similar properties." In the instant 103 rejection, there is express suggestion in the prior art to select primers in the L1 region that detects HPV genotypes. The prior art provides the sequences of the HPV genotypes and alignments of the L1 region. The prior art teaches in designing primers, the efficiency of

amplification is related to the number, position, and stability of a mismatch (Gravitt et al. p. 358 Results 1st paragraph). The prior art teaches primers designed in a conserved region of the L1 region can be used to detect various genotypes of HPV (p. 357 2nd column 1st paragraph). With respect to choosing primers for detection, the prior art (Gelfand et al.) teaches the parameters (i.e. size, parameters, homology) necessary to vary to achieve specific primers. Therefore the prior art teaches the region, the alignment, and the parameters to make and use primers from the L1 region to detect HPV genotypes.

It is prima facie obvious without secondary considerations that with the art teaching the region, the alignment, and the parameters that one skilled in the art would make primers equivalent to SEQ ID No. 1 and 8. The combination provides guidance on making primers for HPV detection from the L1 region, the alignment of HPV genotypes of the L1 region, and guidance for parameters needed for primer design, therefore, the combination suggests primers which are equivalent to SEQ ID No. 1 and 8. The combination is not simply an obvious to try to make the claimed invention; rather there is a reasonable expectation of success. Design of primer pairs is routine in the art and merely constitutes optimization, which is well within the scope of the ordinary artisan. Specific optimization kits, computer programs, and such are in the art, which provide aid to the artisan in primer selection.

The response asserts that the ordinary artisan would not make nondegenrative primers. Gravitt et al. teaches primers with mismatches are less efficient (p. 358 2nd Column 1st Results 1st paragraph). Gravitt et al. teaches differences in type-specific

amplification efficiencies among separate syntheses of degenerate primers (p. 358 1st paragraph). Gravitt et al. teaches to improve the reproducibility and sensitivity by using primers that are not degenerative (p. 358 1st full paragraph). Gravitt et al. teaches primers which do not have degeneracy which are based on sequence alignments of HPV regions (Table 2 p. 359). Therefore it is obvious that the artisan would use the alignment of the L1 region to design primers with as few mismatches as possible and optimization of these primers and primer pairs is routine in the art. Routine optimization is not considered inventive and no evidence has been presented that the primer selection performed was other than routine, that the products resulting form the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Katherine Salmon
Examiner
Art Unit 1634

J. Goldberg
JEANINE A. GOLDBERG
PRIMARY EXAMINER
10/25/06